Melatonin and Zopiclone as Facilitators of Early Circadian Sleep in Operational Air Transport Crews

MICHEL A. PAUL, GARY GRAY, TAREK M. SARDANA, AND ROSS A. PIGEAU

PAUL MA, GRAY G, SARDANA TM, PIGEAU RA. *Melatonin and zopiclone as facilitators of early circadian sleep in operational air transport crews.* **Aviat Space Environ Med 2004; 75:439–43.**

Introduction: This study was an extension into an operational setting of previous laboratory work investigating the use of zopiclone and melatonin to facilitate early circadian sleep in transport aircrew. The previous laboratory-based study demonstrated that both melatonin and zopiclone were effective in inducing early circadian sleep without impacting on psychomotor performance after a 7-h sleep period. ***Methods:*** In a repeated measures, placebo-controlled protocol, 30 aircrew flew 3 transatlantic missions over which they took each of the 3 medications (placebo, sustained-release melatonin 2 mg, or zopiclone 5 mg) at an early body clock time (17:00) during their first stopover. They wore wrist actigraphs prior to and throughout the missions, took a single dose of their scheduled medication immediately prior to their early circadian bedtime, and completed a sleep questionnaire on arising from their medicated sleep. ***Results:*** The results of the actigraphic data show that relative to placebo, aircrew on melatonin and zopiclone fell asleep more quickly (melatonin: $p < 0.01$, zopiclone: $p < 0.003$), slept more (melatonin: $p < 0.02$, zopiclone: $p < 0.005$), had fewer awakenings after sleep onset (melatonin: $p < 0.004$, zopiclone: $p < 0.01$), and spent less time awake after sleep onset (melatonin: $p < 0.01$, zopiclone: $p < 0.05$). The results of the questionnaire data show that relative to placebo, aircrew on melatonin and zopiclone experienced less difficulty getting to sleep (melatonin: $p < 0.0001$, zopiclone: $p < 0.001$), had fewer awakenings (melatonin: $p < 0.005$, zopiclone: $p < 0.001$), less difficulty returning to sleep after awakening (melatonin: $p < 0.0001$, zopiclone: $p < 0.0001$), and reported a better sleep quality (melatonin: $p < 0.0003$, zopiclone: $p < 0.0004$). There were no statistically significant differences between melatonin and zopiclone in any of the actigraphic or questionnaire sleep parameters. ***Conclusions:*** Melatonin and zopiclone, in the dosages we used, are equipotent facilitators of early circadian sleep during transmeridian air transport operations.

Keywords: sleep induction, early circadian sleep, military operations.

OPERATION ALLIANCE, the Canadian Forces airlift that took place in January 1996 in support of Canadian troops in Bosnia, was flown by 18 CC-130 Hercules aircraft carrying out 86 missions from Trenton, Canada, to Split, Croatia, via RAF Lyneham in England, with an aircraft landing in theater every 4 h. During this operation, each crew flew three missions back-to-back before being rotated out of the airlift flow, having flown the maximum allowable flying time per 30 d period of 120 h in as little as 10 to 12 d. There have been anecdotal comments from the participating aircrew as to the severity of fatigue they encountered while at the controls during these missions.

During 10 subsequent resupply missions to Zagreb, Croatia, we monitored aircrew sleep hygiene and in-flight psychomotor performance (13). We documented that the crews commenced these missions with an acute sleep deficit and experienced a fatigue-induced impact on logical reasoning and on a multitask (a simulation of a flying task) toward the end of the outbound transatlantic leg. Further, the crews experienced significant difficulty sleeping at an early circadian time (about 17:00 body clock) in the UK just prior to flying into theater.

In response, we conducted a laboratory-based, placebo-controlled, double-blind repeated measures study to evaluate whether or not melatonin or zopiclone (Imovane®) would facilitate early circadian sleep (9), and whether there would be an effect on performance after a 7-h sleep period. The standard dose of zopiclone is 7.5 mg, although a 5.0 mg dose is available. To date there appears to be no standard melatonin dose, although for advancing or retarding circadian rhythms, the usual dose is 5.0 mg, and for sleep facilitation, the doses typically range from 0.1 to 3.0 mg depending on the formulation (sublingual, tablet, regular release or sustained release, etc). In our laboratory study, to avoid a type II error in assessing performance effects, a high dose of melatonin, 10 mg (5 mg immediate-release plus 5 mg sustained-release Circadin®) and a 7.5-mg dose of zopiclone were used. In that study, both melatonin and zopiclone were equally effective in inducing early circadian sleep, and had no demonstrable effect on performance after the 7-h sleep period. Based on those results we were given permission to conduct an evaluation of these medications during resupply missions to Bosnia. The purpose of this study was to determine whether or not lower doses of sustained release melatonin (Circadin®) and zopiclone would facilitate early circadian sleep as effectively in an operational setting as the higher doses in our laboratory-based study.

From Defence Research and Development Canada-Toronto, North York, Ontario, Canada.

This manuscript was received for review in November 2003. It was revised in January 2004. It was accepted for publication in January 2004.

Address reprint requests to: Michel A. Paul, B.Sc., M.Sc., who is a Defence Scientist at Defence Research and Development Canada-Toronto, 1133 Sheppard Ave. West, P.O. Box 2000, North York, Ontario, Canada M3M 3B9; michel.paul@drdc-rddc.gc.ca.

Reprint & Copyright © by Aerospace Medical Association, Alexandria, VA.

105-05770/

METHODS

After squadron-level briefings, CC-130 aircrew from Canadian Forces 8 Wing at Canadian Forces Base Trenton were asked to participate as subjects in this study during air transport operations to support our troops in Bosnia. The data collection period for this work was run during 27 mo over 70 missions to Zagreb, Croatia, and involved 219 aircrew. The study protocol was approved by the DRDC-Toronto Human Research Ethics Committee. All subjects provided written informed consent according to the declaration of Helsinki. Some aircrew participated in only a single mission. Others participated in 2 missions, while 30 aircrew participated in 3 missions, and, therefore, tried each of the 3 drug conditions (placebo, melatonin, and zopiclone). This manuscript is based on the repeated measures data from the 30 aircrew who participated in 3 missions (1 mission for each drug condition). Of the 30 subjects whose data are reported here, there were 9 male pilots (age 33–41, mean 38.7 ± 2.8 yr), 6 male navigators (age 26–45, mean 33.7 ± 7.6 yr), 5 male flight engineers (age 41–46, mean 43.8 ± 1.9 yr), and 9 male and 1 female loadmasters (age 35–50, mean 40.4 ± 5.2 yr).

The three drug conditions were placebo, zopiclone 5.0 mg (the smallest available clinical dose), and Circadin® 2 mg (a pharmaceutical grade time-released formulation of melatonin made by Neurim Pharmaceuticals in Tel Aviv, Israel). Melatonin is a naturally occurring hormone synthesized by the pineal gland from the precursor amino acid tryptophan (3). Melatonin can advance or retard circadian rhythms depending on the dosage and the timing of ingestion (1,3), and has proven to have a hypnotic effect in a laboratory environment (5,8). Zopiclone (Imovane®) is a cyclopyrrolone derivative with a half-life of approximately 5 h (6,7) that produces a sedative/hypnotic effect. Virtually all studies assessing zopiclone report an effective hypnotic response (2,14). Because melatonin is considered an "investigative new drug" in Canada, regulatory approval from Health Canada was obtained for its use.

The trip itinerary was similar for all missions, and involved an 08:00 departure from Trenton, Ontario, to RAF Lyneham in England, landing anywhere from 02:00 to 04:00 (local). The crews would arrive at their hotel anywhere from 04:00 to 06:00, and retire to bed anywhere from 05:00 to 07:00 h. They would arise between local noon and 14:00 after approximately 7 h of sleep opportunity. Later that evening, the crews would take their scheduled dose of medication and retire around 22:00 local (about 17:00 on their body clocks). On awakening from the medicated sleep, they would complete the medication questionnaire, and return to RAF Lyneham at 08:00 for a round-trip flight to Zagreb, returning to RAF Lyneham at approximately 18:00 to 19:00 (local). After an evening meal, the crews would typically retire between 22:00 and 23:00 local and depart the hotel the next morning about 08:00 local. The crews aimed for a local noon departure from RAF Lyneham, arriving at home base in Trenton, ON, anywhere from 23:00 to 01:00 local time.

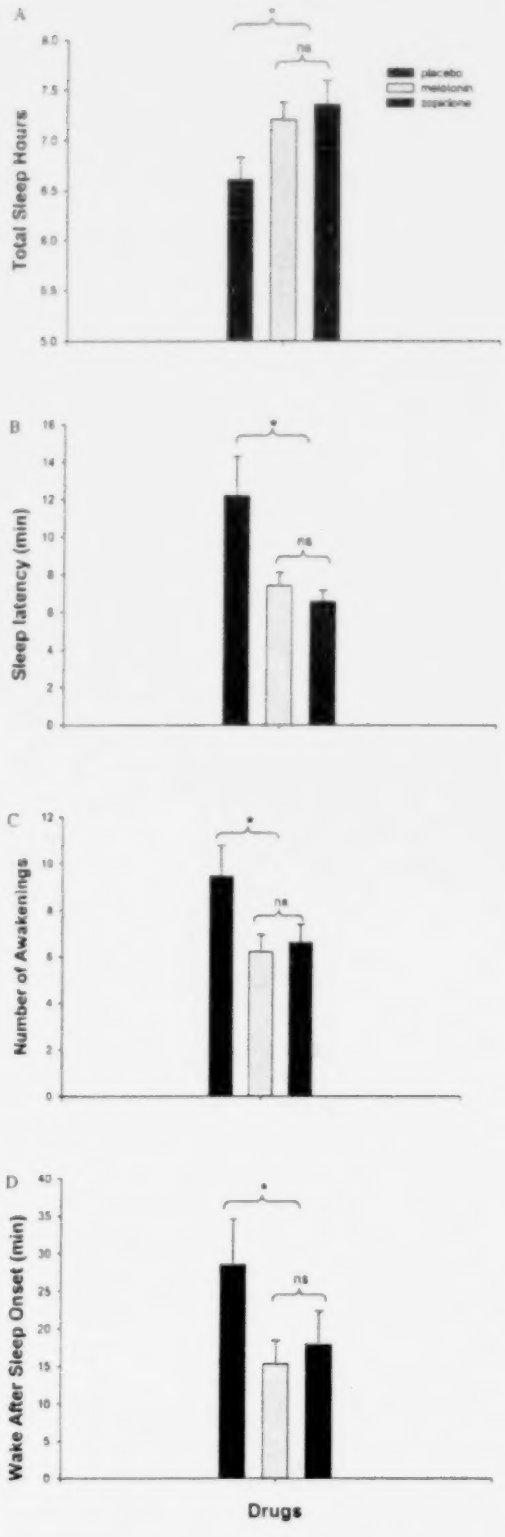
The study protocol was a counterbalanced, placebo-controlled, repeated measures design. In order to maintain the double-blind nature of this work, all medications (placebo, melatonin, and zopiclone) were packaged in identical capsule format. Subjects were not using any medications during these missions other than those prescribed by their flight surgeon. Subjects were asked to abstain from, or at least minimize, alcohol consumption within the current Air Transport regulations (i.e., 12 h from "bottle to throttle"). The subjects recorded their alcohol intake (as part of the medication questionnaire), were compliant with regulations regarding alcohol consumption, and averaged two drinks per 24-h period during off-duty periods.

Further, all participating aircrew took a single dose of their scheduled medication immediately prior to sleep at home, about a week prior to departure for the mission. Subsequent to that dose, before departure on the mission, all participating aircrew were seen by a flight surgeon at Canadian Forces Base Trenton in order to screen out anyone who might have had an idiosyncratic reaction to the medication. No idiosyncratic reactions to the medications were reported, either in the home trials or the operational trials. Because melatonin and zopiclone could be potentially harmful to a fetus (4), any female aircrew who wished to participate was first required to undergo a pregnancy test (from a serum sample) prior to participation on any study mission.

The following measurements/assessments were performed: 1) wrist actigraphy (Precision Control Design, Fort Walton Beach, FL); and 2) questionnaire data soliciting aircrew self-reports of fatigue, sleep quality and mood, drug effects/side effects, and to quantify any alcohol consumed during the mission(s). The crews were issued wrist actigraphs and questionnaires by the study coordinator in Trenton 4 d prior to departure. In order to monitor sleep hygiene before and during the missions, the crews were asked to wear their wrist actigraphs from 3 d prior to the mission until they returned from the mission. The office of the Wing Surgeon (a co-investigator for this study) supervised and coordinated the provision of the mission medications to the aircraft commander on the day of departure. These single doses of medications (2 mg melatonin, or 5 mg zopiclone, or placebo) were taken by the participating crewmember subjects 30 min before retiring to bed for their second sleep overseas. On awakening, each participant completed the questionnaire soliciting their subjective levels of sleep quality by selecting the most appropriate response from 7-point Likert scales. The only extra time commitment for the participating aircrew was the extra few minutes required to complete the questionnaire on awakening from the medicated sleep.

Statistical Analysis

The sleep data gathered from the wrist actigraphs (sleep latency, total sleep time, number of awakenings, wake time after sleep onset) and the questionnaire data (difficulty getting to sleep, # awakenings, difficulty returning to sleep, sleep quality) were plotted for each of the three drug conditions in order to establish the manner in which sleep changed across drug conditions. The sleep and questionnaire data were submitted to a re-



peated-measures analysis of variance. The acceptable level of statistical significance for all main effects or post hoc testing was 0.05.

RESULTS

Actigraphic Assessments of Sleep

The number of hours spent asleep during the medicated sleep in the UK, as well as sleep latency, number of awakenings, and time spent awake after sleep onset, are illustrated in **Fig. 1**. Relative to placebo, subjects slept longer on melatonin ($p < 0.02$) and zopiclone ($p < 0.005$) (Fig. 1a). Their sleep latency was shorter on melatonin ($p < 0.01$) and zopiclone ($p < 0.003$) (Fig. 1b). They had fewer awakenings after sleep onset while on melatonin ($p < 0.004$) and zopiclone ($p < 0.01$) (Fig. 1c) and spent less time awake after sleep onset while on melatonin ($p < 0.01$) and zopiclone ($p < 0.05$) (Fig. 1d). There was no significant difference between melatonin and zopiclone in total sleep time, sleep latency, number of awakenings, or time spent awake after sleep onset.

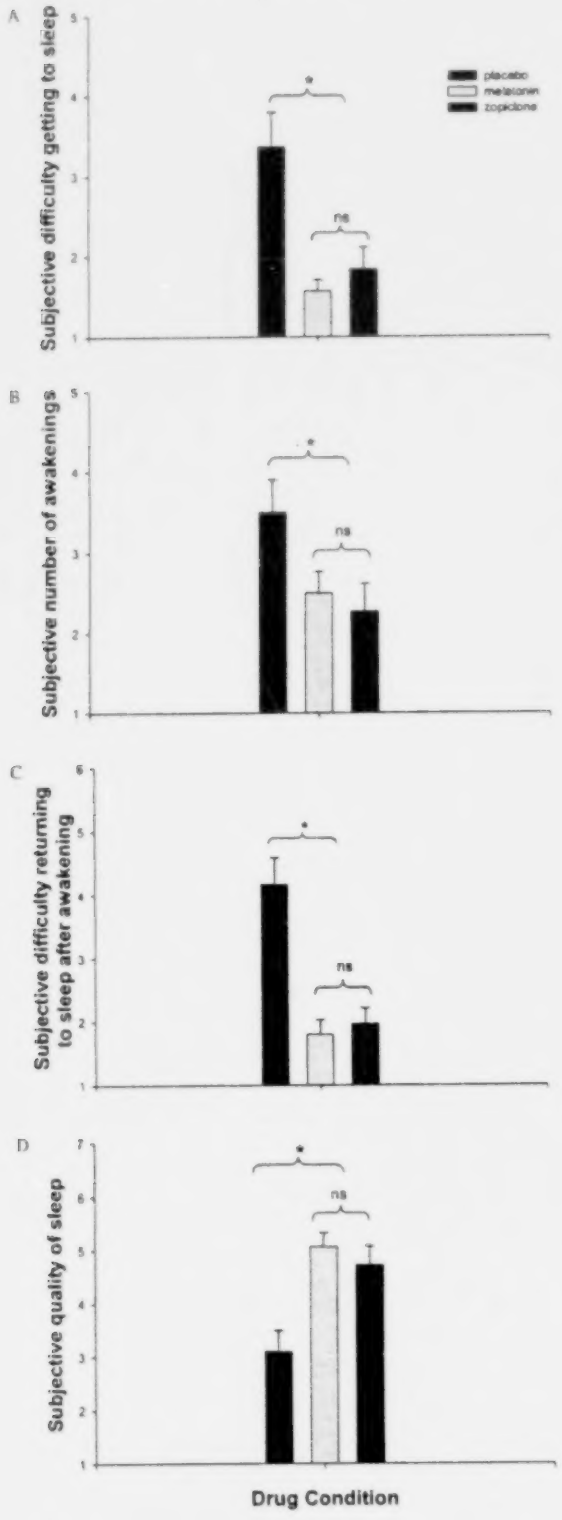
Questionnaire-Based Subjective Assessments of Sleep Quality

Reported difficulty getting to sleep (initial insomnia), reported number of awakenings, difficulty returning to sleep after awakening (middle insomnia), and reported quality of sleep are illustrated in **Fig. 2**. Relative to placebo, the subjects reported less difficulty getting to sleep when they were on melatonin ($p < 0.0001$) and zopiclone ($p < 0.001$) (Fig. 2a). They reported fewer awakenings while on melatonin ($p < 0.005$) and zopiclone ($p < 0.001$) (Fig. 2b), and reported less difficulty returning to sleep after awakening while on melatonin ($p < 0.0001$) and zopiclone ($p < 0.0001$) (Fig. 2c). They also reported a better quality of sleep on melatonin ($p < 0.0003$) and zopiclone ($p < 0.0004$) (Fig. 2d). There was no significant difference between melatonin and zopiclone in difficulty getting to sleep, reported number of awakenings, difficulty returning to sleep after awakening, or quality of sleep.

DISCUSSION

Our initial work during the 10 routine resupply missions to Bosnia demonstrated that our air transport crews began their missions with an acute sleep deficit, resulting in a fatigue-induced impact on psychomotor performance during the outbound transatlantic leg (13). They also had limited sleep in the subsequent two sleep periods during the mission, with the second sleep period resulting in the least amount of sleep during the entire mission. While there was ample opportunity to sleep during the second mission sleep period, the approximate 22:00 bedtime in the UK amounted to an inappropriately early circadian sleep (about 17:00 circadian body clock time), which limited the amount of sleep obtained by the crews.

Fig. 1. Wrist actigraphic values for total sleep hours, sleep latency (min), number of awakenings, and time awake after sleep onset (min) in Figs. 1A, 1B, 1C, and 1D, respectively. All values are mean ± SEM and are plotted over drugs.



In response to the operational difficulties with early circadian sleep, we carried out a laboratory study to determine whether or not melatonin or zopiclone would be effective and safe facilitators of early circadian sleep (9). Our findings indicated that melatonin and zopiclone, in the doses we used, were effective facilitators of early circadian sleep, and after sleep on those medications, there were no negative residual effects on psychomotor performance. The 10-mg total melatonin dose used in the laboratory study was large in order to avoid a type II error where we might conclude that melatonin was safe when in fact it was not. The 7.5-mg dose of zopiclone also used in that work was a standard clinical dose.

The current operational evaluation of these laboratory-proven medications was undertaken to determine whether or not lower doses of melatonin and zopiclone would facilitate early circadian sleep in an operational environment. The 2-mg melatonin (Circadin®) dose was only 20% of the dose used in the laboratory study, whereas the 5-mg zopiclone dose was the smallest clinical dose available and amounted to two-thirds of the dose used in the laboratory study.

The wrist actigraph data from this operational evaluation confirmed that relative to placebo, a 2-mg dose of time-released melatonin (Circadin®) and zopiclone 5 mg were equipotent facilitators of early circadian sleep. Relative to placebo, these doses of melatonin and zopiclone were equipotent in the ability to reduce sleep latency, to reduce the number of awakenings after sleep onset, and to reduce the time spent awake after sleep onset. The questionnaire data from this operational evaluation indicates that aircrew who slept using melatonin or zopiclone reported less difficulty getting to sleep, fewer awakenings, less difficulty returning to sleep, and rated their quality of sleep significantly higher than on placebo.

In a previous laboratory study (9), we demonstrated that a 10-mg melatonin cocktail (5 mg of regular-release melatonin and 5 mg time-released melatonin) and the standard clinical 7.5-mg dose of zopiclone are effective and safe facilitators of early circadian sleep and caused no impact on psychomotor performance after a 7-h sleep period on these medications. The reduced dosages of these medications (2 mg time-released melatonin and 5 mg zopiclone) used in this operational evaluation are also effective facilitators of early circadian sleep.

In our most recent work (10), we compared the effects of zaleplon (marketed as Starnoc® in Canada), zopiclone, temazepam, and melatonin, not on their ability to induce sleep, but for their impact on psychomotor performance after ingestion of a single dose and to quantify respective post-ingestion times to return to normal performance. This study was designed to assess the performance impact of hypnotics that could be used in support of aircrew during air transport operations. Some of the work done by this laboratory over the last

Fig. 2. Subjective scores for difficulty getting to sleep, number of awakenings, difficulty returning to sleep after awakening, and quality of sleep in Figs. 2A, 2B, 2C, and 2D, respectively. All values are mean ± SEM and are plotted over drugs.

7 yr (9–12) has resulted in the Central Medical Board of the Canadian Forces drafting recommendations for new aeromedical policy in support of aircrew during missions which can impact on crew sleep.

These recommendations are based on the laboratory and operational field trials reported in a technical document (11), and are for short-term support (5 d consecutive maximum) of aircrew during operations that can impact on aircrew sleep hygiene. Such pharmaceutical support must be directly under the supervision of a flight surgeon. Prior to any operational use, all aircrew are required to have home trials of any medication listed below in order to preclude any idiosyncratic reactions.

1.) To facilitate sleep when there is a minimum of 8 h before the next duty period, the use of zopiclone (Imovane®) 5 or 7.5 mg is recommended.
2.) If the recall to duty may occur in less than 8 h, but is greater than 3 h, zaleplon (Starnoc®) 10 mg may be used to facilitate sleep. Starnoc® may also be used for longer sleep opportunity windows if preferred by individual aircrew, but because of its shorter action, it is less likely to produce sustained sleep.
3.) Although melatonin shows promise as a sleep aid, it is not yet approved for use in Canada without special approval from Health Canada. The Central Medical Board recommends that Director of Pharmacy Services seek approval from the Health Protection Branch for limited use of melatonin (Circadin® 2 mg) for use by aircrew during layovers to facilitate sleep.

CONCLUSIONS

As an extrapolation from a previous laboratory study (9), the results from the current study indicate that even in an operational setting, melatonin and zopiclone are effective facilitators of early circadian sleep. Furthermore, our recent work (10) has quantified the depth and duration of performance impact due to ingestion of single doses of zaleplon, zopiclone, temazepam, and melatonin. The reader is reminded that these medications are psychotropic in that they can impact on operational performance if military personnel are returned to duty too soon after ingestion. The new aeromedical policy recommendations are based on hard scientific evidence, must be flight-surgeon supervised, and are limited to short-term use (5 d maximum) in aircrew. Chronic use of these medications in aircrew would not be in the best interests of the individual aircrew and would be counterproductive in terms of flight safety.

REFERENCES

1. Arendt J, Aldhous M, English J, et al. Some effects of jet-lag and their alleviation by melatonin. Ergonomics 1987; 30:1379–93.
2. Billiard M, Besset A, de Lustrac C, et al. Effets de la zopiclone sur le sommeil, la somnolence diurne et les performances nocturnes et diurnes chez le volontaire sain. Neurophysiol Clin 1989; 19:131–43.
3. Brown GM. Melatonin in pyschiatric and sleep disorders: Therapeutic implications. Pharmacology and Pathophysiology 1995; 3:209–26.
4. Repchinsky C, ed. Compendium of pharmaceuticals, and specialties. The Canadian drug reference for health professionals. Ottawa, Canada: Canadian Pharmacists Association; 2003:783.
5. Dollins AB, Lynch HJ, Wurtman RJ, et al. Effect of pharmacological daytime doses of melatonin on human mood and performance. Pyschopharmacol 1993; 112:490–6.
6. Gaillot J, Heusse D, Houghton GW, et al. Pharmacokinetics and metabolism of zopiclone. Pharmacology 1983; 27(Suppl 2):76–91.
7. Ladner M, Denny SC. A double-blind study to establish the residual effects of zopiclone on performance in healthy man. In: Nicholson AN, Scholsberg A, Dreyfus JF, eds. Zopiclone: A third generation of hypnotics. Basel, Switzerland: Karger; 1983: 98–108.
8. Lieberman HR, Waldhauser F, Garfield G, et al. Effects of melatonin on human mood and performance. Brain Res 1984; 323: 201–7.
9. Paul MA, Brown G, Buguet A, et al. Melatonin and zopiclone as pharmacologic aids to facilitate crew rest. Aviat Space Environ Med 2001; 72:974–84.
10. Paul MA, Gray G, Kenny G, Pigeau R. Impact of melatonin, zaleplon, zopiclone, and temazepam on psychomotor performance. Aviat Space Environ Med 2003; 74:1263–70.
11. Paul MA, Gray GW, Sardana TM, Pigeau RA. Fatigue countermeasures in support of cf CC-130 air transport operations: From the operation to the laboratory and back to the operation. Ontario, Canada: Defence Research and Development Canada–Toronto; 2003. Report No. TR 2003–106.
12. Paul MA, Pigeau RA, Weinberg H. Human factors of CC-130 operations. Volume 6: Fatigue in long-haul resupply missions. Toronto, Canada: Defence and Civil Institute of Environmental Medicine; 1998. DCIEM Report No.98-R-19.
13. Paul MA, Pigeau RA, Weinberg H. CC-130 pilot fatigue during resupply missions to former Yugoslavia. Aviat Space Environ Med 2001; 72:965–73.
14. Tafti M, Besset A, Billiard M. Effects of zopiclone on subjective evaluation of sleep and daytime alertness and on psychomotor and physical performance tests in athletes. Prog Neuropsychopharmacol Biol Psychiatry 1992; 16:55–63.

DOCUMENT CONTROL DATA SHEET

1a. PERFORMING AGENCY
DRDC Toronto

1b. PUBLISHING AGENCY
DRDC Toronto

2. SECURITY CLASSIFICATION

UNCLASSIFIED
Unlimited distribution -

3. TITLE

(U) MELATONIN and ZOPICLONE as FACILITATORS of EARLY CIRCADIAN SLEEP in OPERATIONAL AIR TRANSPORT CREWS /

4. AUTHORS

Michel A. Paul; Gary W. Gray; Tarek M. Sardana; Ross A. Pigeau

5. DATE OF PUBLICATION

May 1 , 2004

6. NO. OF PAGES

5

7. DESCRIPTIVE NOTES

Published in Aviation, Space, and Environmental Medicine. Vol.75, No. 5. May 2004. Pg 439-443.

8. SPONSORING/MONITORING/CONTRACTING/TASKING AGENCY
Sponsoring Agency:
Monitoring Agency:
Contracting Agency :
Tasking Agency:

9. ORIGINATORS DOCUMENT NO.

Scientific Literature SL 2003-149

10. CONTRACT GRANT AND/OR PROJECT NO.

13if14

11. OTHER DOCUMENT NOS.

13. DOCUMENT ANNOUNCEMENT

Unlimited announcement

14. ABSTRACT

(U) Introduction. This study was an extension into an operational setting of previous laboratory work investigating the use of zopiclone and melatonin to facilitate early circadian sleep in transport aircrew. The previous laboratory based study demonstrated that both melatonin and zopiclone were effective in inducing early circadian sleep without impacting on psychomotor performance after a 7-hour sleep period. Methods. In a repeated measures placebo controlled protocol 30 aircrew flew 3 transatlantic missions over which they took each of the 3 medications (placebo, sustained-release melatonin 2mg, or zopiclone 5 mg) at an early body clock time (1700 hrs) during their first stopover. They wore wrist actigraphs prior to, and throughout the missions, took a single dose of their scheduled medication immediately prior to their early circadian bed-time and completed a sleep questionnaire upon arising from their medicated sleep. Results. Actigraphic data: Relative to placebo, aircrew on melatonin fell asleep more quickly ($p<.01$), slept more ($p<.02$), had fewer awakenings after sleep onset ($p<.004$), and spent less time awake after sleep onset ($p<.01$). On zopiclone they also fell asleep more quickly ($p<.003$), slept more ($p<.005$), had fewer awakenings ($p<.01$) and spent less time awake after sleep onset ($p<.05$). Questionnaire data: Relative to placebo, on melatonin aircrew experienced less difficulty getting to sleep ($p<.0001$), had fewer awakenings ($p<.005$), less difficulty returning to sleep after awakening ($p<.0001$) and reported a better sleep quality ($p<.0003$). On zopiclone, they also reported less difficulty getting to sleep ($p<.001$), fewer awakenings ($p<.001$), less difficulty returning to sleep after awakening ($p<.0001$), and reported a better sleep quality ($p<.0004$). There were no statistically significant differences between melatonin and zopiclone in any of the actigraphic or questionnaire sleep parameters. Conclusions. Melatonin and zopiclone, in the dosages we used are equipotent facilitators of early circadian sleep during transmeridian air transport operations.

(U) Introduction. Cette étude était une extension dans un contexte opérationnel de travaux de laboratoire antérieurs portant sur l'utilisation de la zopiclone et la mélatonine pour faciliter l'induction du sommeil circadien de l'équipage d'aéronef à une heure anticipée. L'étude de laboratoire antérieure avait démontré que la mélatonine et la zopiclone peuvent toutes deux induire efficacement un sommeil circadien anticipée sans toutefois nuire à la performance psychomotrice après une période de sommeil de sept heures. Méthodes. Dans un protocole faisant appel à des mesures répétés et un placebo, 30 équipages d'aéronefs ont effectué trois missions transatlantiques pendant lesquelles ils ont pris chacun des trois médicaments (placebo, 2 mg de mélatonine à libération prolongée et 5 mg de zopiclone) à une heure biologique anticipée (17 h) durant leur première escale. Les membres d'équipage devaient porter un actigraphe au poignet avant le début de la mission et pendant toute la durée de celle-ci, prendre une seule dose du médicament prévu juste avant de se mettre au lit à une heure biologique anticipée et, enfin, remplir un questionnaire sur leur sommeil dès leur réveil après avoir dormi sous l'effet des médicaments. Résultats. Données actigraphiques : Comparativement aux membres qui avaient reçu un placebo, les membres d'équipage qui prenaient de la mélatonine et de la zopiclone s'endormaient plus rapidement (mel $p<.01$, zop $p<.003$), dormaient davantage (mel $p<.02$, zop $p<.005$), s'éveillaient moins souvent après s'être endormis (mel $p<.004$, zop $p<.01$) et passaient moins de temps éveillés après s'être endormis (mel $p<.01$, zop $p<.05$). Données du questionnaire : Comparativement aux membres d'équipage qui recevaient un placebo, ceux qui prenaient de la mélatonine et de la zopiclone avaient moins de difficulté à s'endormir (mel $p<.0001$, zop $p<.001$), se réveillaient moins souvent (mel $p<.005$, zop $p<.001$), avaient moins de difficulté à se rendormir après s'être éveillés (mel $p<.0001$, zop $p<.0001$) et signalaient une meilleure qualité de sommeil (mel $p<.0003$, zop $p<.0004$)). On n'a relevé aucune différence statistiquement significative entre la mélatonine et la zopiclone pour les divers paramètres du sommeil évalués au moyen de l'actigraphe et du questionnaire. Conclusions. Aux posologies que nous avons utilisées, la mélatonine et la zopiclone ont une efficacité équivalente pour ce qui est de faciliter le sommeil circadien anticipé durant les opérations de transport aérien transméridien.

15. KEYWORDS, DESCRIPTORS or IDENTIFIERS

(U) melatonin; zopiclone; early circadian sleep; military operations